```
         51 KSMGLPPRIG SLASGNVRSL PSQQMVNRLS IPKPNLNSTG VNMMSSVHLQ
        101 QNNYGVKSVG QGYSVGQSMR LGLGGNAPVS IPQQSQSVKQ LLPSGNGRSY
                                    ===== ===
        151 GLGSEQRSQA PARYSLQSAN ASSLSSGQLK SPSLSQSQAS RVLGQSSSKP
        201 AAAATGPPPG NTSSTQKWKI CTICNELFPE NVYSVHFEKE HKAEKVPAVA
        251 NYIMKIHNFT SKCLYCNRYL PTDTLLNHML IHGLSCPYCR STFNDVEKMA
        301 AHMRMVHIDE EMGPKTDSTL SFDLTLQQGS HTNIHLLVTT YNLRDAPAES
        351 VAYHAQNNPP VPPKPQPKVQ EKADIPVKSS PQAAVPYKKD VGKTLCPLCF
        401 SILKGPISDA LAHHLRERHQ VIQTVHPVEK KLTYKCIHCL GVYTSNMTAS
        451 TITLHLVHCR GVGKTQNGQD KTNAPSRLNQ SPSLAPVKRT YEQMEFPLLK
        501 KRKLDDDSDS PSFFEEKPEE PVVLALDPKG HEDDSYEARK SFLTKYFNKQ
        551 PYPTRREIEK LAASLWLWKS DIASHFSNKR KKCVRDCEKY KPGVLLGFNM
        601 KELNKVKHEM DFDAEWLFEN HDEKDSRVNA SKTADKKLNL GKEDDSSSDS
        651 FENLEEESNE SGSPFDPVFE VEPKISNDNP EEHVLKVIPE DASESEEKLD
        701 QKEDGSKYET IHLTEEPTKL MHNASDSEVD QDDVVEWKDG ASPSESGPGS
        751 QQVSDFEDNT CEMKPGTWSD ESSQSEDARS SKPAAKKKAT MQGDREQLKW
        801 KNSSYGKVEG FWSKDQSQWK NASENDERLS NPQIEWQNST IDSEDGEQFD
        851 NMTDGVAEPM HGSLAGVKLS SQQA
HITS AT:    126-133

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  133:1200

L5   ANSWER 21 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   270898-03-8  REGISTRY
CN   30: PN: WO0027875 FIGURE: 12 unclaimed sequence (9CI)  (CA INDEX NAME)
CI   MAN
SQL  726

SEQ       1 RSLPSQQMVN RLSIPKPNLN STGVNMMSSV HLQQNNYGVK SVGQGYSVGQ
         51 SMRLGLGGNA PVSIPQQSQS VKQLLPSGNG RSYGLGSEQR SQAPARYSLQ
                    == ======
        101 SANASSLSSG QLKSPSLSQS QASRVLGQSS SKPAAAATGP PPGNTSSTQK
        151 WKICTICNEL FPENVYSVHF EKEHKAEKVP AVANYIMKIH NFTSKCLYCN
        201 RYLPTDTLLN HMLIHGLSCP YCRSTFNDVE KMAAHMRMVH IDEEMGPKTD
        251 STLSFDLTLQ QGSHTNIHLL VTTYNLRDAP AESVAYHAQN NPPVPPKPQP
        301 KVQEKADIPV KSSPQAAVPY KKDVGKTLCP LCYSILKGPI SDALAHHLRE
        351 RHQVIQTVHP VEKKLTYKCI HCLGVYTSNM TASTITLHLV HCRGVGKTQN
        401 GQDKTNAPSR LNQSPSLAPV KRTYEQMEFP LLKKRKLDDD SDSPSFFEEK
        451 PEEPVVLALD PKGHEDDSYE ARKSFLTKYF NKQPYPTRRE IEKLAASLWL
        501 WKSDIASHFS NKRKKCVRDC EKYKPGVLLG FNMKELNKVK HEMDFDAEWL
        551 FENHDEKDSR VNASKTADKK LNLGKEDDSS SDSFENLEEE SNESGSPFDP
        601 VFEVEPKISN DNPEEHVLKV IPEDASESEE KLDQKEDGSK YETIHLTEEP
        651 TKLMHNASDS EVDQDDVVEW KDGASPSESG PGSQQVSDFE DNTCEMKPGT
        701 WSDESSQSED ARSSKPAAKK KGYHAR
HITS AT:    59-66

REFERENCE   1:  133:1200

L5   ANSWER 22 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   270084-38-3  REGISTRY
CN   L-Alanine, L-cysteinyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-
     seryl-L-isoleucyl-L-prolyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   12: PN: US6613740 SEQID: 22 unclaimed protein
```

CN 6: PN: WO0027875 PAGE: 71 unclaimed sequence
SQL 10

SEQ 1 CSALLRSIPA
========
HITS AT: 2-10

REFERENCE 1: 139:208245

REFERENCE 2: 133:1200

L5 ANSWER 23 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **270084-37-2** REGISTRY
CN L-Alanine, L-cysteinyl-L-valyl-L-leucylglycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 11: PN: US6613740 SEQID: 21 unclaimed protein
CN 4: PN: WO0027875 PAGE: 71 unclaimed sequence
SQL 15

SEQ 1 CVLGGGSALL RSIPA
==== =====
HITS AT: 7-15

REFERENCE 1: 139:208245

REFERENCE 2: 133:1200

L5 ANSWER 24 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **223533-74-2** REGISTRY
CN Activity-dependent neurotrophic factor (Mus musculus clone 25 precursor) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 28: PN: WO0027875 FIGURE: 11 unclaimed sequence
CN ADNF (Mus musculus clone 25 precursor)
CI MAN
SQL 828

SEQ 1 MGLPPRISSL ASGNVRSLPS QQMVNRLSIP KPNLNSTGVN MMSNVHLQQN
51 NYGVKSVGQS YGVGQSVRLG LGGNAPVSIP QQSQSVKQLL PSGNGRSFGL
======= =
101 GAEQRPPAAA RYSLQTANTS LPPGQVKSPS VSQSQASRVL GQSSSKPPPA
151 ATGPPPSNHC ATQKWKICTI CNELFPENVY SVHFEKEHKA EKVPAVANYI
201 MKIHNFTSKC LYCNRYLPTD TLLNHMLIHG LSCPYCRSTF NDVEKMAAHM
251 RMVHIDEEMG PKTDSTLSFD LTLQQGSHTN IHLLVTTYNL RDAPAESVAY
301 HAQNNAPVPP KPQPKVQEKA DVPVKSSPQA AVPYKKDVGK TLCPLCFSIL
351 KGPISDALAH HLRERHQVIQ TVHPVEKKLT YKCIHCLGVY TSNMTASTIT
401 LHLVHCRGVG KTQNGQDKTN APSRLNQSPG LAPVKRTYEQ MEFPLLKKRK
451 LEEDADSPSC FEEKPEEPVV LALDPKGHED DSYEARKSFL TKYFNKQPYP
501 TRREIEKLAA SLWLWKSDIA SHFSNKRKKC VRDCEKYKPG VLLGFNMKEL
551 NKVKHEMDFD AEWLFENHDE KDSRVNASKT VDKKHNLGKE DDSFSDSFEH
601 LEEESNGSGS PFDPVFEVEP KIPSDNLEEP VPKVIPEGAL ESEKLDQKEE
651 EEEEEEEDGS KYETIHLTEE PAKLMHDASD SEVDQDDVVE WKDGASPSES
701 GPGSQQISDF EDNTCEMKPG TWSDESSQSE DARSSKPAAK KKATVQDDTE
751 QLKWKNSSYG KVEGFWSKDQ SQWENASENA ERLPNPQIEW QNSTIDSEDG

```
       801 EQFDSMTDGV ADPMHGSLTG VKLSSQQA
HITS AT:    74-81

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  133:1200

REFERENCE   2:  130:306731

L5   ANSWER 25 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   211681-48-0  REGISTRY
CN   Neurotrophic factor ADNF III (mouse gene ADNF III) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   2: PN: WO0027875 SEQID: 3 claimed protein
CN   Neurotrophic factor ADNF III (rat gene ADNF III)
CI   MAN
SQL  806

SEQ      1 MVNRLSIPKP NLNSTGVNMM SNVHLQQNNY GVKSVGQSYG VGQSVRLGLG
        51 GNAPVSIPQQ SQSVKQLLPS GNGRSFGLGA EQRPPAAARY SLQTANTSLP
           ========
       101 PGQVKSPSVS QSQASRVLGQ SSSKPPPAAT GPPPSNHCAT QKWKICTICN
       151 ELFPENVYSV HFEKEHKAEK VPAVANYIMK IHNFTSKCLY CNRYLPTDTL
       201 LNHMLIHGLS CPYCRSTFND VEKMAAHMRM VHIDEEMGPK TDSTLSFDLT
       251 LQQGSHTNIH LLVTTYNLRD APAESVAYHA QNNAPVPPKP QPKVQEKADV
       301 PVKSSPQAAV PYKKDVGKTL CPLCFSILKG PISDALAHHL RERHQVIQTV
       351 HPVEKKLTYK CIHCLGVYTS NMTASTITLH LVHCRGVGKT QNGQDKTNAP
       401 SRLNQSPGLA PVKRTYEQME FPLLKKRKLE EDADSPSCFE EKPEEPVVLA
       451 LDPKGHEDDS YEARKSFLTK YFNKQPYPTR REIEKLAASL WLWKSDIASH
       501 FSNKRKKCVR DCEKYKPGVL LGFNMKELNK VKHEMDFDAE WLFENHDEKD
       551 SRVNASKTVD KKHNLGKEDD SFSDSFEHLE EESNGSGSPF DPVFEVEPKI
       601 PSDNLEEPVP KVIPEGALES EKLDQKEEEE EEEEEDGSKY ETIHLTEEPA
       651 KLMHDASDSE VDQDDVVEWK DGASPSESGP GSQQISDFED NTCEMKPGTW
       701 SDESSQSEDA RSSKPAAKKK ATVQDDTEQL KWKNSSYGKV EGFWSKDQSQ
       751 WENASENAER LPNPQIEWQN STIDSEDGEQ FDSMTDGVAD PMHGSLTGVK
       801 LSSQQA
HITS AT:    52-59

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  133:1200

REFERENCE   2:  129:185098

L5   ANSWER 26 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   211681-43-5  REGISTRY
CN   Neurotrophic factor ADNF III (human gene ADNF III) (9CI)  (CA INDEX NAME)
CI   MAN
SQL  800

SEQ      1 MVNRLSIPKP NLNSTGVNMM SSVHLQQNNY GVKSVGQGYS VGQSMRLGLG
        51 GNAPVSIPQQ SQSVKQLLPS GNGRSYGLGS EQRSQAPARY SLQSANASSL
           ========
       101 SSGHLKSPSL SHSQASRVLG QSSSKPAAAA TGPPPGNTSS TQKWKICTIC
       151 NELFPENVYS VHFEKEHKAE KVPAVANYIM KIHNFTSKCL YCNRYLPTDT
       201 LLNHMLIGHL SCPYCRSTFN DVEKMAAHMR MVHIDEEMGP KTDSTLSFDL
```

```
       251 TLQQGSHTNI HLLVTTYNLR DAPAESVAYH AQNNPPVPPK PQPKVQEKAD
       301 IPVKSSPQAA VPYKKDVGKT LCPLCFSILK GPISDALAHH LRERHQVIQT
       351 VHPVEKKLTY KCIHCLGVYT SNMTASTITL HLVHCRGVGK TQNGQDKTNA
       401 PSRLNQSPSL APVKRTYEQM EFPLLKKRKL DDDSDSPSFF EEKPEEPVVL
       451 ALDPKGHEDD SYEARKSFLT KYFNKQPYPT RREIEKLAAS LWLWKSDIAS
       501 HFSNKRKKCV RDCEKYKPGV LLGFNMKELN KVKHEMDFDA EWLFENHDEK
       551 DSRVNASKTA DKKLNLGKED DSSSDSFENL EEESNESGSP FDPVFEVEPK
       601 ISNDNPEEHV LKVIPEDASE SEEKLDQKED GSKYETIHLT EEPTKLMHNA
       651 SDSEVDQDDV VEWKDGASPS ESGPGSQQVS DFEDNTCEMK PGTWSDESSQ
       701 SEDARSSKPA AKKKATMQGD REQLKWKNSS YGKVEGFWSK DQSQWKNASE
       751 NDERLSNPQI EWQNSTIDSE DGEQFDNMTD GVTEPMHGSL AGVKLSSQQA
HITS AT:    52-59

REFERENCE   1:  133:1200

REFERENCE   2:  129:185098

L5   ANSWER 27 OF 33  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   211439-12-2  REGISTRY
CN   L-Glutamine, L-asparaginyl-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-
     prolyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   10: PN: US6613740 SEQID: 65 unclaimed protein
CN   12: PN: WO2004060309 SEQID: 2 claimed protein
CN   14: PN: WO2004080957 SEQID: 2 claimed sequence
CN   169: PN: WO0053803 SEQID: 4 unclaimed sequence
CN   180: PN: WO0053803 SEQID:2 unclaimed sequence
CN   23: PN: WO0027875 PAGE: 85 unclaimed sequence
CN   5: PN: US20030166544 SEQID: 4 claimed protein
CN   NAPVSIPQ
CI   COM
SQL  8

SEQ      1 NAPVSIPQ
           ========
HITS AT:    1-8

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  141:289067

REFERENCE   2:  141:254386

REFERENCE   3:  141:201591

REFERENCE   4:  141:134117

REFERENCE   5:  141:64409

REFERENCE   6:  141:17925

REFERENCE   7:  140:175485

REFERENCE   8:  140:37325

REFERENCE   9:  140:36048
```

REFERENCE 10: 139:301799

L5 ANSWER 28 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **211439-10-0** REGISTRY
CN L-Serine, L-seryl-L-valyl-L-arginyl-L-leucylglycyl-L-leucylglycylglycyl-L-asparaginyl-L-alanyl-L-prolyl-L-valyl-L-seryl-L-isoleucyl-L-prolyl-L-glutaminyl-L-glutaminyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 24: PN: WO2004080957 SEQID: 12 claimed sequence
CN 2: PN: US6613740 SEQID: 12 unclaimed protein
CN 8: PN: WO2004060309 SEQID: 5 claimed protein
SQL 18

SEQ 1 SVRLGLGGNA PVSIPQQS
== ======
HITS AT: 9-16

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 133:233267

REFERENCE 7: 129:185098

L5 ANSWER 29 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **209051-27-4** REGISTRY
CN L-Alanine, L-valyl-L-α-glutamyl-L-α-glutamylglycyl-L-isoleucyl-L-valyl-L-leucylglycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 16: PN: WO2004080957 SEQID: 4 claimed sequence
CN 1: PN: WO2004060309 SEQID: 15 claimed protein
CN 8: PN: US20030166544 SEQID: 7 claimed protein
SQL 19

SEQ 1 VEEGIVLGGG SALLRSIPA
==========
HITS AT: 11-19

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:207807

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 134:120910

REFERENCE 7: 133:233267

REFERENCE 8: 129:63101

L5 ANSWER 30 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **209051-20-7** REGISTRY
CN L-Alanine, glycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 20: PN: WO2004080957 SEQID: 8 claimed sequence
CN 5: PN: WO2004060309 SEQID: 19 claimed protein
CN 6: PN: US20030166544 SEQID: 5 claimed protein
SQL 10

SEQ 1 GSALLRSIPA
==========
HITS AT: 2-10

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:207807

REFERENCE 4: 136:1116

REFERENCE 5: 134:198025

REFERENCE 6: 134:120910

REFERENCE 7: 133:233267

REFERENCE 8: 129:63101

L5 ANSWER 31 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **188781-55-7** REGISTRY
CN L-Leucine, L-valyl-L-leucylglycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl-L-alanyl- (9CI) (CA INDEX NAME)
SQL 15

SEQ 1 VLGGGSALLR SIPAL
===== ==== =
HITS AT: 6-14

REFERENCE 1: 126:259561

L5 ANSWER 32 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **177718-96-6** REGISTRY
CN L-Alanine, L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
L-Alanine, N-[1-[N-[N-[N2-[N-[N-(N-L-seryl-L-alanyl)-L-leucyl]-L-leucyl]-L-

arginyl]-L-seryl]-L-isoleucyl]-L-prolyl]-
OTHER NAMES:
CN 11: PN: WO2004060309 SEQID: 1 claimed protein
CN 13: PN: WO2004080957 SEQID: 1 claimed sequence
CN 168: PN: WO0053803 SEQID: 3 unclaimed protein
CN 179: PN: WO0053803 SEQID: 1 unclaimed protein
CN 19: PN: US6613740 SEQID: 36 unclaimed protein
CN 4: PN: US20030166544 SEQID: 3 claimed protein
CN 7: PN: WO03063759 SEQID: 7 claimed protein
CN 8: PN: WO0027875 PAGE: 72 unclaimed protein
CN Activity-dependent neurotrophic factor peptide-9
CN Activity-dependent neurotropic factor peptide-9
CI COM
SQL 9

SEQ 1 SALLRSIPA
========
HITS AT: 1-9

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 142:17815

REFERENCE 2: 141:289067

REFERENCE 3: 141:201591

REFERENCE 4: 141:134117

REFERENCE 5: 141:64409

REFERENCE 6: 140:37325

REFERENCE 7: 139:208245

REFERENCE 8: 139:207807

REFERENCE 9: 139:163579

REFERENCE 10: 138:282681

L5 ANSWER 33 OF 33 REGISTRY COPYRIGHT 2005 ACS on STN
RN **177159-38-5** REGISTRY
CN L-Alanine, L-valyl-L-leucylglycylglycylglycyl-L-seryl-L-alanyl-L-leucyl-L-leucyl-L-arginyl-L-seryl-L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 13: PN: US6613740 SEQID: 23 unclaimed protein
CN 15: PN: WO2004080957 SEQID: 3 claimed sequence
CN 6: PN: WO03063759 SEQID: 6 claimed sequence
CN 7: PN: WO0027875 PAGE: 72 unclaimed sequence
CN 9: PN: WO2004060309 SEQID: 14 claimed protein
CN Activity-dependent neurotrophic factor-14
CN ADNF 14
SQL 14

SEQ 1 VLGGGSALLR SIPA

HITS AT: 6-14

REFERENCE 1: 141:289067

REFERENCE 2: 141:134117

REFERENCE 3: 139:208245

REFERENCE 4: 139:163579

REFERENCE 5: 136:1116

REFERENCE 6: 134:198025

REFERENCE 7: 134:120910

REFERENCE 8: 133:233267

REFERENCE 9: 133:145193

REFERENCE 10: 133:99660

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 10:38:48 ON 24 FEB 2005)
L6 9 S L5
L7 9 DUP REM L6 (0 DUPLICATES REMOVED)

L7 ANSWER 1 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:428956 BIOSIS
DOCUMENT NUMBER: PREV200400430460
TITLE: Protective peptides that are orally active and mechanistically nonchiral.
AUTHOR(S): Brenneman, Douglas E. [Reprint Author]; Spong, Catherine Y.; Hauser, Janet M.; Abebe, Daniel; Pinhasov, Albert; Golian, Tania; Gozes, Illana
CORPORATE SOURCE: Drug Discovery, Johnson and Johnson Pharmaceut Res and Dev LLC, Welsh and McKean Rd, Spring House, PA, 19477, USA dbrennem@prdus.jnj.com
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (June 1 2004) Vol. 309, No. 3, pp. 1190-1197. print. ISSN: 0022-3565 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Nov 2004
Last Updated on STN: 10 Nov 2004

AB Previous reports identified two peptides that mimic the action of neuroprotective proteins derived from astrocytes. These peptides, NAPVSIPQ and SALLRSIPA, prevent neuronal cell death produced by electrical blockade, N-methyl-D-aspartate, and beta-amyloid of NAPVSIPQ and SALLRSIPA were synthesized and compared respectively to the corresponding all L-amino acid peptides. In rat cerebral cortical test cultures cotreated with 1 muM tetrodotoxin, the D-amino acid peptides produced similar potency and efficacy for neuroprotection as that observed for their respective L-amino acid peptides. Since all these peptides tested individually exhibited attenuation of efficacy at concentrations of >10 pM, combinations of these peptides were tested for possible synergies.

Equimolar D-NAPVSIPQ and D-SALLRSIPA combination treatment produced potent neuroprotection (EC50, 0.03 fM) that did not attenuate with increasing concentrations. Similarly, the combination Of L-NAPVSIPQ and D-SALLRSIPA also had high potency (EC50, 0.07 fM) without attenuation of efficacy. Combined administration of peptides was tested in a model of fetal alcohol syndrome and in a model of learning impairment: apolipoprotein E knockout mice. Intraperitoneal administration Of D-NAPVSIPQ Plus D-SALLRSIPA to pregnant mice (embryonic day 8) attenuated fetal demise after treatment with an acute high dose of alcohol. Furthermore, oral administration Of D-NAPVSIPQ Plus D-SALLRSIPA significantly increased fetal survival after maternal alcohol treatment. Apolipoprotein E knockout mice injected with D-NAPVSIPQ Plus D-SALLRSIPA showed improved performance in the Morris water maze. These studies suggest therapeutic potential for the combined administration of neuroprotective peptides that can act through a mechanism independent of chiral recognition.

L7 ANSWER 2 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:394427 BIOSIS
DOCUMENT NUMBER: PREV200400394878
TITLE: NAP mechanisms of neuroprotection.
AUTHOR(S): Gozes, Illana [Reprint Author]; Steingart, Ruth A.; Spier, Avron D.
CORPORATE SOURCE: Sackler Fac MedDept Clin Biochem, Tel Aviv Univ, IL-69978, Tel Aviv, Israel
igozes@post.tau.ac.il
SOURCE: Journal of Molecular Neuroscience, (2004) Vol. 24, No. 1, pp. 67-72. print.
ISSN: 0895-8696 (ISSN online).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Oct 2004
Last Updated on STN: 6 Oct 2004

AB An 8-amino-acid peptide, NAPVSIPQ (NAP), was identified as the smallest active element of activity-dependent neuroprotective protein that exhibits potent neuroprotective action. Potential signal transduction pathways include cGMP production and interference with inflammatory mechanisms, tumor necrosis factor-alpha, and MAC1-related changes. Because of its intrinsic structure, NAP might interact with extracellular proteins and also transverse membranes. NAP-associated protection against oxidative stress, glucose deprivation, and apoptotic mechanisms suggests interference with fundamental processes. This paper identifies p53, a key regulator of cellular apoptosis, as an intracellular target for NAP's activity.

L7 ANSWER 3 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:202994 BIOSIS
DOCUMENT NUMBER: PREV200400203537
TITLE: Neuronal cell death produced by electrical blocakde is prevented by an ADNP peptide (NAP) : structure - activity studies with an alanine scan.
AUTHOR(S): Brenneman, D. E. [Reprint Author]; Spong, C. Y. [Reprint Author]; Hauser, J. M. [Reprint Author]; Gozes, I.; Wilkemeyer, M. F.; Charness, M. E.
CORPORATE SOURCE: Lab. Developmental NeuroBiol., NICHD, Bethesda, MD, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 676.5.

http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

AB Activity-dependent neuroprotective protein (ADNP) is a glia-derived protein that contains a bioactive peptide fragment: NAPVSIPQ (NAP). Neuroprotective properties have been demonstrated for synthesized NAP that include prevention of neuronal cell death from beta amyloid peptide, hydrogen peroxide, and electrical blockade with tetrodotoxin (TTX). Dose response studies to NAP produce a bimodal response with EC50's of 3 fM and 3 pM in preventing neuronal death after TTX treatment. In the present study, peptide analogs were prepared to perform a systematic alanine scan of NAP in TTX-treated cerebral cortical cultures. The aim was to identify critical amino acid residues that are essential to the complex, neuroprotective pharmacology of NAP. Substitutions with alanine at Ser-5 and Pro-7 completely inactivated the protective action of the peptide. Alanine substitutions at Pro-3, Val-4 and Iso-6 did not affect efficacy, but significantly decreased potency by 3-4 orders of magnitude at the fM site. At the pM site, alanine substitutions at Pro-3 and Iso-6 produced 2-3 orders of magnitude decrease in potency. Substitution at Asn-1 produced a small decrease in efficacy and 33-fold decrease in potency at both sites. These studies indicate that a C-terminal portion of NAP (SIP) is essential for full efficacy of the peptide's neuroprotective properties against TTX at both sites. Except for Gln-8, none of the amino acids are mutable to alanine while maintaining full activity of the peptide. Furthermore, the bimodal neuroprotective activity and the differential response for each peak of activity relative to the structural changes made in NAP strongly suggest multiple mechanisms of action.

L7 ANSWER 4 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:202380 BIOSIS
DOCUMENT NUMBER: PREV200400202923
TITLE: NAP, a femtomolar - acting neuroprotective peptide stabilizes microtubules by direct association with tubulin: toward clinical development.
AUTHOR(S): Dvinski, I. N. [Reprint Author]; Spier, A. D.; Gozes, I. [Reprint Author]
CORPORATE SOURCE: Dept. of Clin. BioChem., Sackler Sch. of Med., Tel Aviv, Israel
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 629.15.
http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

AB The peptide NAP (NAPVSIPQ) efficiently protects neurons against a wide

variety of insults in vivo and in vitro. Now, cell survival-screening assays indicate that NAP has cell specific properties protecting pheochromocytoma (PC12) cells against oxidative stress (10-17 M to10-10 M), but not NIH-3T3 fibroblasts. Further studies utilizing 1) affinity chromatography of brain extracts and 2) dot blot analysis, identified tubulin and actin, the brain major cytoskeletal proteins, as NAP-binding ligands. When added to PC12 cells, or cerebral cortical astrocytes and neurons, NAP (10-15 M to 10-10 M) induced a rapid microtubular re-organization into distinct microtubular structures that were identified by immunostaining with monoclonal anti-tubulin antibodies and confocal microscopy. Fluoresceine-labeled NAP induced similar cytoskeletal changes and was detected in the intra-cellular milieu, even when incubated at 40C or at low pH. These results indicate that NAP crosses the plasma membrane and induces microtubular re-organization: A mechanism that may be related to NAP's cell protective activities. NAP's bioavailability relies in part on its primary structure that shows similarity to proteins that can traverse the plasma membrane. In GLP repeated-escalating dose toxicology studies with administration via the intransal route, no NAP toxicity has been observed (>1000x effective concentration, rats and dogs). Pharmacokinetic assessments include mass spectrometry. NAP is positioned for clinical development.

L7 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:519889 BIOSIS
DOCUMENT NUMBER: PREV200100519889
TITLE: Neurotrophic peptide exhibits stability in vivo and in vitro.
AUTHOR(S): Hauser, J. M. [Reprint author]; Gozes, I.; Furman, S.; Giladi, E.; Rubinraut, S.; Fridkin, M.; Spong, C. Y. [Reprint author]; Brenneman, D. E. [Reprint author]
CORPORATE SOURCE: LDN, NICHD-NIH, Bethesda, MD, USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 949. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2001
Last Updated on STN: 23 Feb 2002

AB NAP, an eight amino acid peptide (NAPVSIPQ), is derived from activity-dependent neuroprotective protein, a glial protein regulated by vasoactive intestinal peptide. NAP exhibits neuroprotection from toxins at femtomolar levels in cell culture. Administration (IP) to pregnant mice prevents fetal death in a model of fetal alcohol syndrome. Intranasal treatment produces neuroprotection from cholinotoxicity in adult rats. In the current study, the stability of NAPVSIPQ (propyl 3-3,4-3H) was assessed in vitro and in vivo using reverse phase and size exclusion chromatography. Addition of labeled NAP to serum-containing growth medium of cerebral cortical cultures resulted in 95% of the labeled peptide co-migrating with intact peptide at 3 hours incubation and 90% at 6 hours. In vivo, tissues were sampled for labeled NAP 60 min after administration. After IP injection to pregnant mice on gestational day 8, 39% of the total radioactivity recovered in the fetus co-migrated with

intact peptide. In maternal cortex, 2% of the recovered labeled material co-migrated with intact peptide. Similarly, intranasal administration of labeled peptide to adult rats also resulted in 2% of the peptide in brain co-migrating with intact NAP (JPET 293:1091, 2000). These studies indicate that NAP is unusually stable in complex biological systems, and that it effectively penetrates fetal and brain barriers. The natural stability of this neuroprotective peptide coupled with its high potency supports further investigation of NAP as a therapeutic agent.

L7 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:144204 BIOSIS
DOCUMENT NUMBER: PREV200200144204
TITLE: Oral prenatal treatment with peptides increases adult performance in a learning paradigm.
AUTHOR(S): Spong, Catherine [Reprint author]; Vink, Joy; Auth, Jonathan; Gozes, Ilana; Brenneman, Douglas
CORPORATE SOURCE: NICHD, NIH, SDMP, LDN and PPB, Bethesda, MD, USA
SOURCE: American Journal of Obstetrics and Gynecology, (December, 2001) Vol. 185, No. 6 Supplement, pp. S243. print.
Meeting Info.: 22nd Annual Meeting of the Society for Maternal-Fetal Medicine. New Orleans, Louisiana, USA. January 14-19, 2002. Society for Maternal-Fetal Medicine.
CODEN: AJOGAH. ISSN: 0002-9378.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 26 Feb 2002

L7 ANSWER 7 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:160809 BIOSIS
DOCUMENT NUMBER: PREV200100160809
TITLE: Prevention of alcohol-induced proinflammatory cytokine release and spatial learning deficits with novel peptides in a mouse model of fetal alcohol syndrome.
AUTHOR(S): Spong, C. Y. [Reprint author]; Auth, J. [Reprint author]; Vink, J.; Abebe, D. T.; Gozes, I.; Brenneman, D. E.
CORPORATE SOURCE: National Institutes of Health, SDMP, LDN, NICHD, Bethesda, MD, USA
SOURCE: American Journal of Obstetrics and Gynecology, (January, 2001) Vol. 184, No. 1, pp. S22. print.
Meeting Info.: 21st Annual Meeting of the Society for Maternal-Fetal Medicine. Reno, Nevada, USA. February 05-10, 2001. Society for Maternal-Fetal Medicine.
CODEN: AJOGAH. ISSN: 0002-9378.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2001
Last Updated on STN: 18 Feb 2002

AB OBJECTIVE: To evaluate the release of proinflammatory cytokines in fetal alcohol syndrome (FAS) and the effect of the peptides, NAPVSIPQ (NAP) and SALLRSIPA (SAL) in modulating their release. Because cytokines have known effects on long-term potentiation, a model of learning at the molecular level, we evaluated learning in adult offspring. Previously NAP+SAL prevented alcohol-induced fetal death, growth abnormalities, and oxidative

damage in this FAS model. METHODS: A well-characterized FAS mouse model was used. On day 8, pregnant mice were injected with alcohol (0.03 mL/kg) or placebo. Pretreatment with the peptides NAP+SAL (20 mug) or placebo was given 30 minutes before alcohol. For cytokine analysis, embryos were removed after 6 hours and analyzed (ELISA) for tumor necrosis factor (TNF-alpha) and interleukin-6 (IL-6). To assess learning, adult male offspring were tested in the Morris watermaze evaluating latency to find a hidden platform. RESULTS: TNF-alpha was significantly elevated in alcohol vs control (50.0 +- 3.5 vs 32.7 +- 2.4 pg/mL, P = .001). NAP + SAL pretreatment prevented the alcohol-induced increase (39.9 +- 2.8 pg/mL, P=.01) with levels not different than control (P = .1). Similarly, IL-6 was elevated in alcohol vs control (22.6 +- 1.4 vs 17.3 +- 0.6 pg/mL, P = .001); NAP + SAL prevented the alcohol-induced increase (19.1 +- 1.0, P = .02), with levels similar to control (P = .2). In the Morris watermaze, the alcohol-treated litters exhibited no evidence of learning over the 7d trial. In contrast, the control litters decreased their latency 50% by the fifth day (P=.001). The learning curve of NAP + SAL + alcohol litters was not different than that of control at all time points tested. CONCLUSIONS: The peptides NAP + SAL attenuate alcohol-induced increases in proinflammatory cytokines and prevent alcohol-induced performance deficits in a learning paradigm. These data suggest that NAP + SAL provide protective efficacy through cytokine-mediated mechanisms.

L7 ANSWER 8 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:204012 BIOSIS
DOCUMENT NUMBER: PREV200100204012
TITLE: A novel VIP responsive gene: Activity dependent neuroprotective protein.
AUTHOR(S): Gozes, I. [Reprint author]; Zamostiano, R.; Pinhasov, A.; Bassan, M.; Giladi, E.; Steingart, R. A.; Brenneman, D. E.
CORPORATE SOURCE: Department of Clinical Biochemistry, Tel Aviv University, Tel Aviv, 69978, Israel
igozes@post.tau.ac.il
SOURCE: Fahrenkrug, Jan; Said, Sami I. Ann. N. Y. Acad. Sci., (2000) pp. 115-118. Annals of the New York Academy of Sciences. VIP, PACAP, GLUCAGON, and related peptides: Fourth International Symposium. print.
Publisher: New York Academy of Sciences, 2 East 63rd Street, New York, NY, 10021, USA. Series: Annals of the New York Academy of Sciences.
Meeting Info.: Fourth International Symposium on VIP, PACAP, Glucagon, and Related Peptides. Elsinore, Denmark. September 02-04, 1999.
CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 1-57331-273-8 (cloth), 1-57331-274-6 (paper).
DOCUMENT TYPE: Book
Conference; (Meeting)
Book; (Book Chapter)
Conference; (Meeting Paper)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2001
Last Updated on STN: 19 Feb 2002

L7 ANSWER 9 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:129398 BIOSIS
DOCUMENT NUMBER: PREV200000129398

TITLE: Activity-dependent neurotrophic factor-14 requires protein kinase C and mitogen-associated protein kinase kinase activation to protect the developing mouse brain against excitotoxicity.

AUTHOR(S): Gressens, Pierre [Reprint author]; Marret, Stephane; Bodenant, Corinne; Schwendimann, Leslie; Evrard, Philippe

CORPORATE SOURCE: INSERM E 9935, Hopital Robert-Debre, Paris, France

SOURCE: Journal of Molecular Neuroscience, (Aug.-Oct., 1999) Vol. 13, No. 1-2, pp. 199-210. print.
CODEN: JMNEES. ISSN: 0895-8696.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Apr 2000
Last Updated on STN: 4 Jan 2002

AB Activity-dependent neurotrophic factor (ADNF) is a newly identified compound that prevents in vitro neuronal death when present in fentomolar concentrations. ADNF-14, a 14 amino acid peptide derived from ADNF, has the same effects on growth as the parent molecule. However, the transduction pathways and target cells for these highly potent trophic factors are still unknown. We previously described a mouse model of excitotoxic lesions of the developing neocortex mimicking several hypoxic or hypoxic-like brain lesions observed in human fetuses and neonates. In this model, cotreatment with the excitotoxin ibotenate and ADNF-14 prevented both neuronal death in pups injected on the day of birth and white matter cystic lesions in pups treated 5 d after birth. In the present study, coadministration of ibotenate, ADNF-14, and selective transduction pathway inhibitors showed that activation of protein kinase C (PKC) and mitogen-associated protein kinase kinase was critical for neuroprotection. Immunocytochemistry revealed that ADNF-14 activated PKC and mitogen-associated protein kinase in cortical neurons on the day of birth and in white matter astrocytes on the fifth postnatal day. Taken in concert, these data identify PKC and mitogen-associated protein kinase pathways as critical to ADNF-14-induced neuroprotection of the developing brain against excitotoxic damage.

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